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(2S,4S)-3-((1R)-1-hydroxyethyl)-2-azetidinone derivs. prodn. -  
comprises reducing corresp. 3-acetyl deriv. in presence of NADP  
oxido-reductase

Patent Assignee: MERCIAN CORP (SAOC )

Number of Countries: 001.. Number of Patents: 002

Abstract (Basic): JP 4054182 A'

Prodn. of (3S, 4S)-3-((1R)-1-hydroxyethyl) -2-azetidinone derivs. of  
formula (I) comprises reducing (3S, 4S)-3-acetyl-2-azetidinone derivs. of  
formula (II) in presence of a NADP oxidoreductase produced by Streptomyces  
omiyensis; where R1 and R2 = H, lower alkyl, phenyl, benzyl or  
diphenylmethyl, or together form lower alkylene; Z = H or amino-protecting  
gp.

The oxidoreductase is produced by Streptomyces omiyensis W-4028  
(FERM P-11210) isolated from the soil of Kumamoto Pref., Japan, which may  
be incubated in a medium contg. glycerol, meat extract, polypeptone, yeast  
extract, NaCl, MgSO4.H2O CaHPO4, CaCO3 (precipitate), and defoaming agent,  
at 28 deg. C.

The redn. is carried out with the cells or their processed ones of  
Str. omiyensis in an aq. medium (buffer soln.) at a temp. of 20-35 deg.  
C, pref. 25-30 deg. C, at pH 5-9, pref. pH 6-8, for a period of 3-48 hrs..  
The prod. is extracted with a solvent, e.g. toluene, Et2O, CHCl3, EtOAc,  
BuOAc.

USE/ADVANTAGE - (I) are known as intermediates for beta-lactam  
antibiotics, e.g. formimidoylthienamycin (imipenem). The invention  
provides a new process for stereospecifically reducing (II) to (I) in high  
purity and high yield.

In an example, a soln. of 100 mg/ml (3S,4S)-3-acetyl-4-  
-((1S)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-(4-methoxyphenyl) -2-azetidinone  
in CHCl3 (1 ml each) was placed in a 500 ml flask (x 3) and CHCl3 was  
evapd. by blowing nitrogen gas to form thin film on the bottom of flask.  
Then, the cultured broth of Str. omiyensis (250 ml each) was added and  
shaken at 28 deg. C for 24 hrs. n-BuOAc (50 ml) was added and the flask  
was shaken vigorously. The mixt. was centrifuged (2350 rpm, 10 mins, 10  
deg. C) and the upper layer was washed with aq. NaCl, dried and evapd. to  
give 900 mg residue, which was chromatographed on a silica gel column  
(toluene/EtOAc=4/1) to give 333.9 mg  
(3S,4S)-3-((1R)-hydroxyethyl)-4-((1S)-2,2-dimethyl  
-1,3-dioxolan-4-yl)-1-(4-methoxyphenyl) -2-azetidinone.

Dwg. 0/0

Title Terms: HYDROXYETHYL; AZETIDINONE; DERIVATIVE; PRODUCE; COMPRISE; REDUCE;  
CORRESPOND; ACETYL; DERIVATIVE; PRESENCE; NADP; OXIDO; REDUCTASE

Derwent Class: B03

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; C12N-009/04; C12R-001/46; C12P-017/16; C12R-001-465